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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference Case 21416	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/10683	International filing date *(day/month/year)* 25.09.2003	Priority date *(day/month/year)* 27.09.2002
International Patent Classification (IPC) or both national classification and IPC C12N9/00		
Applicant DSM IP ASSETS B.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09.03.2004	04.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Maddox, A Telephone No. +31 70 340-2336

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/10683

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-37 as originally filed

Sequence listings part of the description, Pages

1-33 as originally filed

Claims, Numbers

1-26 as originally filed

Drawings, Sheets

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority in written form.

   ☒ furnished subsequently to this Authority in computer readable form.

   ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 26

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 26

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-25
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-25
Industrial applicability (IA)	Yes:	Claims	1-25
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The ISA found the that the application lacked unity of invention and invited the applicant to pay an additional search fee. The applicant elected not to pay this fee. The International Search Report has therefore been established for the subject matter as indicated under item V of the present written opiinion. The remaining unsearched subject matter is not examined (Article 17(2)(a) or (3) and Rule 66.1(e) PCT)

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 The subject matter under examination relates to claims 1-25 concerning polynucleotide sequences encoding acetyl-CoA carboxylase and uses thereof.

2 The following documents are relevant, the numbering will be maintained.

D1: WO9932635
D2 :EP1035206
D3: EP1158051
D4: WO0011199

3 **Novelty and Inventive step**

3.1 D1 discloses DNA sequences encoding an acetyl CoA carboxylase (ACC) enzyme from Candida albicans, having 55% amino acid identity with SEQ ID NO:3 underlying claims 1-3. In the absence of any further definition of the levels of identity mentioned in claims 1(e), 2(p) and 3, the subject matter can not be distinguished from that of D1. Furthermore claims 1 and 2 lack clarity to such an extent, for example 1(i) and 2(t) extend to any 15nts and 1(d) and 2(o) to any nucleotide, that no difference can be determined between the claimed subject matter and that of D2 and D3 as well as D1. Both D2 (cf. SEQ ID NOS. 1 and 2) and D3 (cf. SEQ ID NOS:1 and 2) disclose sequences useful in astaxanthin production in Phaffia. Hence the application does not meet the requirements of Article 33(2) PCT because the subject matter of claims 1-3 is not new.

3.1.1 The subject matter of claims 4-25 taken in combination with claims 1-3 does not meet the requirements of Article 33(2) and (3) PCT in that it is either not new, or lacks inventive step in that it represents routine design alternatives known to the skilled person, by comparison to D1-D3.

3.2 Even if novelty could be established for certain subject matter it would nevertheless lack an inventive step for the following reasons. D1 discloses sequences for an ACC enzyme isolated from the yeast Candida. The sequences encode a protein with high identity (55% amino acid) to the putative ACC of the present application. D1 represents the closest state of the art. The subject matter of the application, as claimed in claims 1-3, differs from that of D1 in that it represents different ACC sequences. No surprising effect can be associated with these differences. The problem faced by the skilled person is the provision of alternative ACC sequences. The skilled person would have been aware of the teaching of D1 and would find incentive to search for other ACC sequences in the normal course of investigation. The skilled person would therefore arrive at the sequences of the present application by a process of arbitrary selection devoid of any inventive skill or ability above that to be expected. The sequences of the invention therefore lack an inventive step within the meaning of Article 33(3) PCT

3.2.1 The remaining embodiments, as claimed in claims 4-25 do not involve an inventive step since they relate to obvious design alternatives or uses suggested from the state of the art. For example the antisense ACC approach has been suggested for increasing carotenoid levels from D4 (cf. claims 9,10,21, and 24).

4 Clarity

4.1 Notwithstanding the equivocal nature of the individual elements thereof, claims 1 and 2 effectively relate to a multiplicity of independent claims, the extent and nature of which results in a lack of clarity in the claimed subject matter as a whole, since the skilled person is unable to determine the differences between the plurality of claimed embodiments. The application therefore does not meet the requirements of Article 6 PCT.

4.2 Claims 6,10,16, and 20-22 relate to products, vector and recombinant organisms, defined by a product of manufacture. Since sequences may be lost from vectors and vectors from hosts this method of claiming does not adequately define the subject matter of the invention in terms of its essential technical features. Moreover it is unclear how the technical features of claim 22 concerning **antisense technology, site-directed mutagenesis, error prone PCR, or chemical mutagenesis** relate to the introduction of the previously defined vector. The same objections also arise in claims 23-25. The methods of claims 23-25 relate to the production of carotenoids. Naturally occurring Phaffia have different levels of ACC and produce carotenoids such as astaxanthin. Claims 23-25 therefore do not recite the invention in terms of the essential technical features thereof.